polymethoxyflavone selected from the group consisting of 5,6,7,8,4'-pentamethoxyflavone, 5,6,7,8,3',4'-hexamethoxyflavone, heptamethoxyflavone, sinensetin, tetra-O-methyl-scutellarein, 5-desmethylsinensetin and mixtures thereof.--

--19. (Newly added) The method of claim 13 wherein said polymethoxyflavone is 5,6,7,8,4'-pentamethoxyflavone.--

--20. (Newly added) The method of claim 13 wherein said polymethoxyflavone is 5-desmethylsinensetin.--

--21. (Newly added) The composition of claim 16 wherein said polymethoxyflavone is 5,6,7,8,4'-pentamethoxyflavone.--

--22. (Newly added) The composition of claim 16 wherein said polymethoxyflavone is 5-desmethylsinensetin.--

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REMARKS

Claims 1-12 have been canceled without prejudice or disclaimer. Applicants reserve the right to file one or more continuation or divisional applications directed to the canceled subject matter. New claims 13-22 have been added. The subject matter of the amendments to the claims is fully supported in the specification as originally filed. See specifically Example 1 and pages 7-8 and 10-11 of the present specification. No new matter has been added.

The rejection of claims 1-12, as it now pertains to new claims 13-22, under 35 USC 103(a) as being unpatentable over Cook

et al., Nutritional Biochemistry, pp66-76, 1996 in combination with Robbins, U.S. Patent No. 3,867,541 is respectfully traversed. The Office states that Claims 1-8 are drawn to a method of reducing the level of substances in a mammal which contribute to cardiovascular diseases or disorders comprising administering an effective amount of a polymethoxyflavone to reduce the production of substances in a mammal which contribute to cardiovascular diesases and/or disorders. It then states that claims 9-12 are drawn to polymethoxyflavone compositions suitable for reducing the level of substances in a mammal which contribute to cardiovascular diseases. The Office states the Cook teaches that there is significant inverse association between dietary flavonoid intake and mortality from coronary heart diease (CHD) via administration of flavonoids such as polyhydroxyflavones. The Office also states that Cook teaches that flavonoids act as inhibitors of low density lipoprotein (LDL) oxidation and platelet aggregation, two conditions that contribute to atherosclerosis or cardiovascular disease. The Office then states that although Cook teaches flavones broadly as well as hydroxylated flavones, the reference does not specifically teach the use of methoxylated flavones, nor the specific methoxyflavones as claimed in the present application.

With respect to Robbins, the Office states that the Robins reference bridges the nexus between the invention and the prior art as it teaches that methoxylated flavonoid compositions such as sinensetin and limocitrin (refers to column 11, line 30 and column 4, llines 10-68) exhibit strong anti-adhesive effects on blood cells which may show clinically that they are useful as antithrombogenic agents. The Office further states that Robbins teaches that the blood aggregation can cause infarction of vital

organs citing column 9, lines 4-15. which inherently teaches the use of these compounds in compositions for the treatment of coronary artery disease and supports the use of the methoxylated form of flavones. The Office then states that Applicant has set forth compositions wherein known polymethoxyflavones are combined for reducing the level of substances which contribute to cardiovascular diseases or disorders. It then states that the combination of two compounds known to achieve effect in a composition is seen as obvious, unless there is some unexpected result. It also states the prior art has clearly set forth the blood cell activity anti-adhesive/anti-aggregate quality of methoxylated flavonoids having at least two methoxy substituents such as sinensetin and limocitrin.

The Office concludes that it would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention was made to use a polymethoxyflavone in a composition for reducing the level of substances that contribute to cardiovascular diseases or disorders. The Office further concludes that a person of ordinary skill in the art would have been motivated to use a polymethoxyflavone in a composition for reducing the level of substances that contribute to cardiovascular diseases or disorders given that the prior art has set forth that flavones, specifically polyhydroxy or polymethoxyflavones can act as inhibitors of substances which contribute to CHD, such as LDL oxidation and platelet aggregation. The Office finally concludes that it is *prima facie* obvious to combine two compounds each of which is taught by prior art to be useful for same purpose in order to form a composition that is to be used for very same purpose.

Applicants respectfully submit that the combination of Cook

in view of Robbins fails to render the instantly claimed invention *prima facie* obvious. Cook taken in view of Robbins fails to teach compositions or methods for reducing the levels of Apolipoprotein B production by providing an apolipoprotein B reducing amount of a polymethoxyflavone as set forth in the presently claimed invention. Cook taken in view of Robbins fails to motivate one of ordinary skill in the art to practice the method of the presently claimed invention using the compositions of the presently claimed invention because the combination of references fails to teach a method for reducing apolipoprotein B production and compositions for achieving apolipoprotein B reduction.

The Office is using the improper standard of obvious to try. It is respectfully submitted that the essence of obviousness does not arise by merely picking and choosing from the prior art to produce the claimed invention. "In order to establish *prima facie* obviousness it is necessary for the examiner to present evidence preferably in the form of some teaching, suggestion, incentive, or general available knowledge, that one of ordinary skill in the art would have been led to combine relevant teachings of the applied references in the proposed manner to arrive at the claimed invention. Ex parte Levengood, 28 USPQ2d 1300, 1301 (Bd. Pat. & Int'f, 1993). Starting from this correct standard of obviousness, the error of the Office is clear-the rejection is improper because the Office has failed to identify any teachings in the prior art motivating the skilled artisan to to produce the method and compositions of the presently claimed invention. No references or combination of references have been provided which would teach, suggest, or motivate one of ordinary skill in the art to modify the Cook taken in view of Robbins to

use polymethoxyflavones of any type to reduce apolipoprotein B production. There is simply no motivation save for the teachings of the inventor's application, to produce the claimed invention. The Office is also using the improper standard of ***IMPROPER*** hindsight analysis. It is impermissible to use the claimed invention as an instruction manual or template to piece together the teachings of the prior art so that the claimed invention is rendered obvious. One cannot use improper hindsight reconstruction to pick and choose among isolated disclosures in the prior art to deprecate the claimed invention. Cook taken in view of Robbins fails to render the instantly claimed invention *prima facie* obvious.

Furthermore, the Office states that Robbins inherently teaches the use of methoxylated flavonoid compositions such as sinensetin and limocitrin for the treatment of coronary artery disease and supports the use of methoxylated form of flavones. Consideration of an inherent quality is relevant only to anticipation, not obviousness (Jones v. Hardy, 230 USPQ 1021, 1025, Fed. Cir., 1984).

Therefore, Applicant respectfully submits that no *prima facie* case of obviousness has been established and the instant rejection be withdrawn.

In the event this paper is deemed not timely filed, the undersigned petitions for an appropriate extension of time. Please charge any fees which may be required by this paper or at any time during prosecution of the instant application, or credit any overpayment, to deposit account 50-2134.

Respectfully Submitted

March 4, 2003
DATE

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CERTIFICATE OF FILING VIA FACSIMILE

The undersigned hereby certifies that the attached **Amendment with Marked up Version to Show Changes Made with a petition for a three (3) month extension of time** were this day March 4, 2003, filed in the United States Patent and Trademark Office via facsimile to facsimile number 703-308-4556 Pages: 11

Gail E. Poulos

VERSION WITH MARKINGS TO SHOW CHANGES MADE

IN THE CLAIMS:

Claims 1-12 have been canceled without prejudice or disclaimer.

New claims 13-22 have been added.